

Implementing Encapsulated Nanodroplet Crystallisation Techniques to Crystallise Natural Products

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Natural products are a rich source of inspiration for the development of new medicines. Natural products and their derivatives have been used to treat a host of diseases and conditions, such as pain management, cancer, heart disease and infection.[1, 2] In fact, more than 50 % of small molecule drugs developed in the United States between 1981–2014 were derived from natural products or semisynthetic derivatives.[2] However, absolute structure determination of new bioactive molecules – an essential step in the development of a clinical drug – remains a time-consuming practical impediment. Therefore, methods to increase the speed at which the 3D molecular structure of an unknown natural product can be solved must be developed in order to alleviate this “bottleneck” in the discovery process of clinical compounds.

Herein, we report the successful deployment of a new crystallisation approach to rapidly access crystals of complex organic molecules that are otherwise challenging to crystallise (including natural products). Using encapsulated nanodroplet crystallisation (ENaCt) protocols, a significant number of natural products have been structurally characterised crystallographically.[3] The structures of these molecules have been unambiguously confirmed by single crystal X-ray diffraction analysis, both at Newcastle University and through collaboration with the UK National Crystallography Service and Diamond Light Source. The first results of this highly successful proof of concept project are soon to be published, thus allowing other groups to apply our approaches to related problems, particularly in cases where traditional solution phase characterisation techniques yield ambiguous results which require further verification.

References

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